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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/622,727 | 07/21/2003 | Jacques Bartholeyns | 0508-1011-1 | 2789 |
| 466 | 7590 | 07/02/2007 | | |
| YOUNG & THOMPSON 745 SOUTH 23RD STREET 2ND FLOOR ARLINGTON, VA 22202 | | | EXAMINER YU, MISOOK | |
| | | | ART UNIT 1642 | PAPER NUMBER |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|---|--|
| Office Action Summary | Application No. 10/622,727 | Applicant(s) BARTHOLEYNS ET AL. | |
| | Examiner MISOOK YU | Art Unit 1642 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 March 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 6-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Claims 7-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-21 are pending and claims 1-6 are under consideration.

Claim Rejections - 35 USC § 112, Maintained

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant argues that the amended claim 5 is definite. Since applicant has not disputed the Office's interpretation of claim 5 in the previous Office action i.e. "the cells being used in claim 5 further limits the cells of the base claim to be cells cultured for 5-10 days", the Office still maintains the rejection because the limitation "further" in line 2 of claim 5 indicates the scope of the claim to be interpreted as two different ways: first is that claim 5 is drawn to administration of the specifically made monocytes with the specifically recited method steps in claim 5 in addition to the monocytes being administered in claim 1 (note the limitation "further comprising" in claim 5); and the second is that the scope of the claim 5 is that the "monocytes" being administered in

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claim 1 is prepared by the method step in claim 5. In other words, there is no additional monocytes in claim 5.

Claim Rejections - 35 USC § 103, Maintained

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, and 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bartoleyns et al (IDS, Immunobiology, 1996, vol. 195, pages 550-562).

Claims 1, 2, and 4-6 are drawn to method of treating cancer using monocyte derived cells and chemotherapy, wherein the monocyte derived cells and chemotherapy administered simultaneously (claim 2), in injection form (claim 4), the monocyte derived cells are cultured for 5-10 days (claims 5 and 6).

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bartoleyns et al (IDS, Immunobiology, 1996, vol. 195, pages 550-562) as applied to claim 1 above, and further in view of Gehl et al (Seminars in Oncology, vol. 23, No. 6, Supp 15, December 1966, pages 35-38).

Claim 3 is drawn to method of cancer treatment using monocyte derived cell and various art-known chemotherapeutic agents, and taxol being one of them.

Response to Arguments

The declaration under 37 CFR 1.132 filed 03/02/2007 is insufficient to overcome the rejection of claims based upon Claims 1, 2, and 4-6 as set forth in the last Office action. Applicant's argument along with Dr. Dupuy's declaration have been fully considered but found unpersuasive for the following reasons:

Applicant argues "In a preferred embodiment, the two active ingredients are administered simultaneously and are in the form of an injectable solution". This argument has been fully considered but not persuasive because the argument is not commensurate in scope of claims. Only claim 2, the two active ingredients are administered simultaneously, only claim 4 is, the two active ingredients in the form of an injectable solution. No claim says "the two active ingredients are administered simultaneously and are in the form of an injectable solution"

Applicant reviews what Bartoleyns et al., teach at page 8 of the remark section, and then at the last paragraph at page 8 argues that "This article does not disclose any therapy including the administration in a patient of an effective amount of monocyte derived cells (i.e., a cell distinct from activated macrophages) and an effective amount of chemotherapy drugs as recited in claim 1'. This argument has been fully considered but found unpersuasive because the data used in Dr. Dupuy's declaration under 37 CFR 1.132 filed 03/02/2007 also uses activated macrophages as the monocyte derived cells. Note the paragraph bridging pages 2-3 the declaration.

Applicant further argues that "There would be no motivation to modify BARTHOLEYNS to arrive at the recited method. When reading the article of

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BARTHOLEYNS, a person skilled in the art of treating cancer would immediately think about the apparent contradiction of administering a cellular preparation (e.g. monocyte derived cells) along with a treatment designed to limit or stop the cell-life (e.g. chemotherapy). Indeed, one would expect chemotherapy to limit growth or kill the monocyte derived cells. Therefore, the general assertion made in the Official Action does not constitute a serious motivation for combining chemotherapy and cellular therapy as claimed in the present invention.” These arguments have been fully considered but found unpersuasive because Bartoleyns et al., teach method of treating cancer using monocyte derived cells (i.e. activated macrophages, note Table 1 at page 553), and also suggest reducing tumor burden by chemotherapy prior to administration of the immunotherapy (i.e. macrophage). Note the instant claims 1-6 are not limited to administration conditions (10^9 MAK cells and 1.0mmh MDX-H210 are mixed and administered) set forth in Dr. Dupuy’s declaration. Therefore, this argument is considered as arguing limitation not present in the claims. because if tumor, reducing tumor burden before immunotherapy would in of the immune response against established tumor might only be successful the immune response against established tumor might only be successful. The specification does not define the scope of the limitation “simultaneously”. The specification as originally filed does not define the limitation to be the same condition as in Dr. Dupuy’s declaration. As for claim 4, the injectable form could be in separate vials instead of the mixed condition in Dr. Dupuy’s declaration.

Applicant also argues that “the combination of macrophages and cisplatin allows suppressing the cells resistance to the chemotherapeutic drug. This is surprising because of the possible cytotoxic effect of cisplatin on the macrophages themselves, which was not observed the conditions of the invention. Furthermore, the combination of chemotherapeutic drugs and activated macrophages allows to solve the acute problem of drug resistance in cancer treatment by chemotherapy.” These arguments have been fully considered but found unpersuasive, because the argument with the combination of macrophages and cisplatin is not commensurate in scope of the claims because the scope is much broader and it is not applicable to the genus of the claimed invention. As for argument with “drug resistance”, applicant is arguing a limitation not present in the claims. One of ordinary skill would be motivated to use monocyte derived cells (i.e. activated macrophages) in combination with other art-known chemotherapy with a reasonable expectation of success for cancer therapy since the efficacy of monocyte derived cells is taught in Bartoleyns et al., and Bartoleyns et al., suggest chemotherapy to reduce the tumor burden for stimulation of immune response by monocyte derived cells.

As for claim 3, applicant argues that “a person skilled in the art would not have combined the teachings of BARTHOLEYNS and a chemotherapy drug, such as those of GEHL, for treating cancer”. This argument has been fully considered but found unpersuasive because one of ordinary skill would be motivated to use monocyte derived cells (i.e. activated macrophages) in combination with taxol with a reasonable

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expectation of success for cancer therapy since the efficacy of monocyte derived cells is taught in Bartoleyns et al., and Bartoleyns et al., suggest chemotherapy to reduce the tumor burden for stimulation of immune response by monocyte derived cells, and Gehl et al teach that taxol is well known chemotherapeutic agent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MISOOK YU
Primary Examiner
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/Misook Yu/